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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,837	10/29/2001	Masakazu Kobayashi	212653	1504

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EXAMINER
MERTZ, PREMA MARIA

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 03/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/889,837	KOBAYASHI ET AL.	
	Examiner	Art Unit	
	Prema M Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 12/23/03

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-10, 13 is/are pending in the application.

4a) Of the above claim(s) 4, 5, is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-3, 6-10, 13 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group 1 (claims 1-3, 6-10, 13) on 12/23/03 is acknowledged. The traversal is on the ground(s) that the restriction is improper since the examiner has not shown that examination of Groups I and II would entail a serious burden. This is not found persuasive because a search for a method of suppressing ongoing acute allograft rejection comprising administering an IL-10 antibody of Group I would not necessarily reveal art for a method of suppressing ongoing acute allograft rejection comprising administering an IL-10 receptor antibody and therefore the searches for the 2 Groups would not overlap.

The PCT rules define a special technical feature as a feature, which defines a contribution over the prior art. The first claimed invention fails to recite such a feature, since the methods are practiced with materially different products, an IL-10 antibody in Group I and an IL-10 receptor antibody in Group 2, which products are structurally and chemically different, the novelty of the inventions lying in the products being administered and not the processes. The only feature in common in the instant inventions is a method of suppressing ongoing acute allograft rejection" which does not constitute the special technical feature lacking from the prior art because this method can be used with a composition other than the instant products such as an antisense oligonucleotide specific for IL-10 mRNA (see WO 97/31532, abstract cited in prior office action). Distinctness is further shown because each of these products in each method can be made and used without any one or more of the other products. The products used in each of the methods of Groups I and II are physically, chemically and biologically distinct from each other, and if patentable would support separate patents.

The Groups as delineated in the restriction requirement of 11/6/2003 are patentably distinct one from the other such that each invention could, by itself, in principle, support its own separate patent (as shown by the arguments put forth in the written restriction requirement).

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-2, 7-10 and 13 will be examined insofar as they encompass a method of suppressing ongoing acute allograft rejection by administering an antibody to IL-10.

Claims 4-5 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. It is suggested that the title be amended to recite "method of suppressing ongoing acute allograft rejection by administering an IL-10 antibody and cyclosporin A".

3. For the instant application which is claiming benefit under 35 U.S.C. 371 of a prior application, which in turn claims the benefit of a provisional application under 35 U.S.C. 119(e), Applicants are requested to insert the continuing data in the first line of the specification, under "Reference to Cross-related Applications", "This application is a 371 of PCT/US00/01553, filed 1/21/2000, which claims the benefit of U.S. Provisional Application No. 60/116,845, filed 1/22/1999."

Claim Rejections - 35 USC § 112, first paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 6-10 and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of suppressing ongoing acute allograft rejection, which method comprises administering to a host experiencing ongoing acute allograft rejection an IL-10 antibody and cyclosporin A, in amounts effective to rescue the allograft from ongoing acute rejection, does not reasonably provide enablement for a method as recited in claims 1 and 13 in which an IL-10 inhibitor and an IL-2 inhibitor are administered. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1 and 13 encompass a method of suppressing ongoing acute allograft rejection, which method comprises administering to a host experiencing ongoing acute allograft rejection all IL-10 inhibitors and all IL-2 inhibitors. Claims 1 and 13 are clearly single means claims (M.P.E.P. 2164.08(a)) because the specification has only enabled a method of suppressing ongoing acute allograft rejection, which method comprises administering to a host experiencing ongoing acute allograft rejection an IL-10 antibody and cyclosporin A. A single means claim, i.e., where a means recitation does not appear in combination with another recited element of means, is subject to an undue breadth rejection under 35 U.S.C. 112, first paragraph. *In re Hyatt*, 708 F.2d 712,714 - 715, 218 USPQ 195, 197 (Fed. Cir. 1983) (A single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification disclosed at most only those means known to the

inventor). When claims depend on a recited property (result), a fact situation comparable to *Hyatt* is possible, where the claims cover every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. See M.P.E.P. 2164.08(a).

Since no material limitations, for example, for the IL-10 inhibitor have been recited in the claim, claim 1, encompasses every conceivable structure (means) for achieving the stated property (result), a fact situation comparable to *Hyatt*. The claimed invention encompasses a method of administering compositions not envisioned or described in the specification, and neither does the specification disclose how these claimed compositions could be distinguished from each other. The specification on page 9, lines 16-28, discloses administering IL-10 antagonists such as antibodies to IL-10 receptor and mutant IL-10 ligands. However, in Example 7, page 18, the specification only enables a method of administering IL-10 antibody and cyclosporin A to achieve the desired result. By application of the factors set forth in *Ex parte Forman* (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure, in the instant application, the quantity of experimentation to determine which other IL-10 inhibitors are encompassed by the scope of the claims is practically infinite and the guidance provided in the specification very little. Therefore, it would require undue experimentation to determine which IL-10 inhibitors having the desired biological activity would be encompassed by the scope of the claims. The disclosure of a

method of using an IL-10 antibody is clearly insufficient support under the first paragraph of 35 U.S.C. § 112 for claims, which encompass administering all IL-10 inhibitors. In *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), the Courts have held that:

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since some improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that the scope of the claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Therefore, there are substantial scientific reasons to doubt the scope of enablement, as set forth above. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. With respect to claim 13, Applicants are claiming a method in which due to insufficient immunosuppression by an IL-2 inhibitor, an IL-10 inhibitor is then administered to achieve the desired suppression of ongoing acute allograft rejection. The specification does not describe administering any other IL-10 inhibitor and IL-2 inhibitor other than IL-10 antibody and cyclosporin A, respectively, and since it is deemed to constitute undue experimentation to determine all the others that can be used in the instant method, the disclosure is not

commensurate with the scope of the claims. With respect to claim 13, Applicants are claiming a method in which due to insufficient immunosuppression of ongoing acute allograft rejection by an IL-2 inhibitor, an IL-10 inhibitor is then administered to achieve the desired suppression of ongoing acute allograft rejection. However, as asserted above, Applicants are not enabled for a method in which anything less than an IL-10 antibody and cyclosporin A are employed in the instant method. It is suggested that by employing conventional claim language, the claims be amended to include the specific inhibitors supported by the instant specification.

Furthermore, IL-10 is secreted by Th2 cells, the target cells of IL-10 being macrophages, in which IL-10 suppresses cytokine production and thus indirectly reduces cytokine production by Th1 cells (see page 309, last 5 lines of Table, Goldsby et al., 2000). The reference also teaches that Th1 cells are directly involved in graft rejection (see page 524, column 2, first 4 lines of first full para). From the prior art teachings inhibiting IL-10 bioactivity by administering an IL-10 antibody would not be expected to treat acute graft rejection. Therefore, Applicants are only enabled for a method of suppressing ongoing acute allograft rejection, which method comprises administering to a host experiencing ongoing acute allograft rejection an IL-10 antibody and cyclosporin A as demonstrated in the instant application.

Claim rejections-35 USC § 112, second paragraph

5. Claim 6 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6, line 2, is indefinite in the recitation of "blocks the upstream or downstream signals of IL-10". This language is vague and indefinite because it is unclear what "the upstream

signal of IL-10" is. Page 9, lines 20-21, recites this limitation, however, there is no definition in the specification of "the upstream signal of IL-10".

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (571) 271-0871.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Prema Mertz

Prema Mertz Ph.D.
Primary Examiner
Art Unit 1646
February 17, 2004